HIGH ENERGY SYNTHETIC COMPOUNDS FOR FUTURE COMPACT COMBAT RATIONS

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INTRODUCTION

Of the many problems of concern in designing compact combat rations, one of the most perplexing is how to achieve maximum caloric density within the tight limits of weight and volume prescribed for such rations. The problem is compounded by strict nutritional requirements. For example, there is a limitation on the amount of fat that can be incorporated in the ration since an excess of fat in the diet adversely affects health. Because fats are dense in calories, this delimitation of their use handicaps the designer of compact combat rations. One approach to the solution of this problem is the substitution of high-energy compounds for most of the carbohydrates in the diet. This approach has been explored at the U.S. Army Natick Laboratories, and research to find and synthesize high caloric, non-lipid compounds has progressed to the point where three model compounds (1,3-butanediol, propylene glycol, and glycerol) were investigated for use in supplying dietary calories in high-energy rations. While the compounds studied may not be used, it is reasonable to believe that this new approach can make a substantial contribution not only to the development of future compact combat rations, but also to the design of rations for lunar exploration and other space missions.

Although the possibility of utilizing polyhydric alcohols in nutrition has not been extensively explored, Fischer et al (2), Mayer (3) Schlüssel (5) and Bormmann (4) conducted investigations on pharmacological effects between 1949 and 1955. More recently, Dymsza and Miller (1), in seeking to find and synthesize compounds to replace carbohydrates, examined a number of compounds, eventually selecting 1,3-butanediol as the compound of greatest potential. This work was sponsored by the Air Force at the Massachusetts Institute of Technology. During the past 15 months, at the U.S. Army Natick Laboratories, research on synthetic food compounds has been in progress. Evaluation of 1,3-butanediol has been continued, and in addition, other food compounds have been investigated.

EXPERIMENTAL

Criteria for Selection. The high-energy compounds were selected in accordance with the rather exacting criteria given below:

(a) Capable of being synthesized or obtained by means independent of land cultivation.

(b) Preferably containing more kcal/gm than carbohydrates.

(c) Non-toxic and physiologically harmless.

(d) Capable of replacing a large percentage of the carbohydrates in moderately high-fat diets.

Characteristics of the Compounds Selected: On the basis of the above requirements, three polyhydric alcohols, namely 1,3-butanediol, propylene glycol and glycerol, were selected for the study reported herein. Although glycerol contains only as much kcal/gm as carbohydrates, it was included as a "control" because it can be synthesized and because it is a polyhydric alcohol. All 3 glycols are available commercially at relatively low cost. Some characteristics of the compounds are given in Table 1.

TABLE 1
Some Characteristics of Compounds Evaluated as Food Sources

Compound	kcal/gm[1]	LD_{50}[2] (gm/kg)	Present Use
1,3-Butanediol	6	25	Chemical intermediate, plasticizer, food flavor and color solvent; cosmetic emollient.
Propylene Glycol	5	30	Solvent for flavors and pharmaceuticals, food and tobacco humectant; preservative; treatment of ketosis in dairy cattle; cosmetic emollient.
Glycerol	4	30	Solvent or lubricant in beverages, cosmetics and foods; tobacco humectant.

[1] Estimated metabolizable energy.
[2] Acute single-dose oral toxicity in the rat.

Experimental Diets, Animals and Techniques. Experimental diets were formulated and administered whereby each of the 3 polyhydric alcohols replaced a portion of the common carbohydrates on a caloric equivalent basis. These diets (Table 2) were fed to young laboratory rats (usually 10 per treatment) for 2 to 5 weeks.

TABLE 2
Experimental Diets

	1 10% Fat	2 30% Fat	3 30% Fat + 20% BD	4 30% Fat + 20% PG	5 30% Fat + 20% Glycerol
	%	%	%	%	%
Casein	22.0	22.0	22.0	22.0	22.0
Glucose Monohydrate	19.8	13.0	3.0	3.0	3.0
Sucrose	19.6	13.0	3.0	3.0	3.0
Dextrin	19.6	13.0	3.0	3.0	3.0
Lard	7.5	22.5	22.5	22.5	22.5
Corn Oil	2.5	7.5	7.5	7.5	7.5
1,3-Butanediol	-	-	20.0	-	-
Propylene Glycol	-	-	-	20.0	-
Glycerol	-	-	-	-	20.0
Mineral Mix	4.0	4.0	4.0	4.0	4.0
Vitamin Mix	1.0	1.0	1.0	1.0	1.0
Choline Chloride (50%)	0.4	0.4	0.4	0.4	0.4
Cellulose[1]	3.6	3.6	13.6	13.6	13.6

[1] Increased in diets containing BD, PG and Glycerol in order to make all diets iso-nitrogenous and iso-caloric.

Studies were also conducted on rats fed these compounds under the stress of a cold environment. Animals exposed to cold exhibit a marked increase in food consumption, presumably to meet their elevated caloric demands due to an accelerated metabolism. In addition, numerous tissue lipid changes occur in rats subject to a cold environment, and cold acclimation has a pronounced action on hepatic lipid metabolism. These animals were housed in a thermostatically controlled room maintained at room temperature (25° ± 1°C), medium cold (5° ± 1°C), or severe cold (-10° ± 1°C). Meshed rubber laboratory mats were used to cover the floor bottoms of the cages in the cold rooms. In the survival test used to compare ability to withstand severe cold, rats from each dietary treatment were maintained for 4 weeks at 25°C and 5°C, followed by exposure at -20°C until 50% survived from each group.

To assess BD as an energy source during muscular activity in higher animals, diets containing this compound were fed to adult male Beagles. Six purebred male Beagles were fed the control 30% fat diet (Table 2) for 2 weeks. After this conditioning period, each dog was placed on a treadmill and exercised to exhaustion. The treadmill, placed at an angle of 11°, had a constant speed of 4 mph. After determining baseline performance, three dogs were changed to the 30% fat + 20% BD diet (Table 2); the remaining 3 dogs continued to consume the control diet. The dogs were run again at 1, 3 and 5 weeks after the start of the experimental feeding period.

Blood plasma samples were obtained from each dog before and after its run on the treadmill. Plasma free fatty acids (FFA) were determined by the Kelley (6) modification of the Dole method (7). In another test, plasma glucose was determined at 0, 5, 10, 20, 40 and 80 minutes after treadmill running and finally at the time of exhaustion. The glucose analysis was accomplished with the Technicon Autoanalyzer.

Lipid and Isotope Analyses. Total lipids were determined in liver, muscle and adipose tissue by the chloroform-methanol, sephadex chromatography method of Therriault and Poe (8). Neutral lipids of blood plasma were separated from phospholipids by column chromatography. Quantitative determination of neutral lipid fractions was carried out by thin layer chromatography (TLC) according to the method described by Louis-Ferdinand et al (9).

Since glucose utilization is so vital to the tissues, especially for the metabolism of the brain, initial studies have been conducted on the influence of feeding BD on the metabolism of glucose. Rats fed the BD diet for 3 to 8 months were intubated with 10 microcuries of uniformly labeled Glucose-C^{14}, and placed in a special all-glass metabolism cage for 24 hours. The expired $C^{14}O_2$ was continuously monitored and recorded.

RESULTS AND DISCUSSION

Animal Feeding Study Comparing 1,3-Butanediol (BD), Propylene Glycol (PG) and Glycerol. Fig. 1 shows that lowered 5-week growth rates were obtained in BD fed rats as compared to the rates obtained in rats fed the control diet. However, when the amount of food consumed was related to the 5-week weight gain in terms of food efficiency, as summarized in Table 3, it is apparent that this decreased growth is reflected by a proportionally lowered amount of diet consumed. Food efficiencies of the rats consuming the 30% fat diets were the same regardless of energy source. Therefore, it appears that young rats may limit their consumption of BD or PG containing diet because of taste or palatability, but the calories supplied by these synthetic compounds were efficiently utilized.

TABLE 3
Comparison of Glycols as Food Sources[1]

	1 10% Fat	2 30% Fat	3 30% Fat + 20% BD	4 30% Fat + 20% PG	5 30% Fat + 20% Glycerol
Wt. Gain, g	202	191	140	172	183
Food Intake, g	533	442	337	426	445
Food Efficiency[2]	38	43	42	41	41

[1] 5-week feeding.
[2] Grams body weight gain per gram food intake x 100.

Metabolism of Glucose - C^{14} in BD-Fed Rats. Preliminary results have been obtained on the metabolism of D-Glucose - C^{14} to $C^{14}O_2$ in rats fed diets containing 30% fat and 30% fat + BD. Continuous monitoring of the $C^{14}O_2$ for 24-hour periods from rats intubated with the uniformly labeled glucose indicated that an average of 90% and 77% of ingested activity was recovered in 24 hours in rats fed the BD and the 30% fat control, respectively.

Energy Utilization, Tissue Lipids and Survival Under Cold Stress. Weight gains and total calories consumed by young rats fed for successive 2-week periods at room temperature (25°C) and moderately cold (5°C) are presented in Table 4. Rats pair-fed the 30% fat diets, with and without BD (diets 2 and 3), had statistically similar weight gains within the two environments. These pair-fed groups had a 28% increased food intake in the cold; the ad libitum fed rats (10% fat, diet 1) increased their food intake by 40% in the 5°C environment. This increased level of food consumption with smaller body weight gains, reflects the increased caloric demands of the animals in cold acclimation.

TABLE 4
Average 2-Week Weight Gains and Energy Intake of Rats at Mild (25°) and Moderately Cold (5°) Temperatures

	Treatment	25°		5°	
		Wt gain	Energy Intake	Wt gain	Energy Intake
		g	Total kcal	g	Total kcal
(1)	10% Fat	89.4 ± 2.3^{a}[1]	951	53.7 ± 3.9^{c}	1341
(2)	30% Fat + 20% BD	76.8 ± 4.4^{b}	964	38.0 ± 5.3^{d}	1234
(3)	30% Fat[2]	84.9 ± 4.5^{ab}	974	32.1 ± 3.7^{d}	1250

[1] Mean ± SE. Means having common letter in superscript are not significantly different ($P > 0.05$).
[2] Pair-fed to treatment (2).

The epididymal adipose tissue weight, liver lipids, and liver cholesterol of rats fed the 3 polyols and maintained at temperate and cold environments for 4 weeks are presented in Table 5. All animals had reduced adipose tissue pads when exposed to the cold; however, rats fed the glycols, BD and PG, had significantly ($P < 0.05$) lowered adipose tissue weight than did the controls or glycerol fed animals at both environments.

Liver lipids and liver cholesterol were significantly ($P < 0.05$) higher in rats fed PG at 25°C than in any of the other treatments. Cold reduced both the lipid and cholesterol content of the livers of rats fed PG. In the present study cold had no effect on the liver cholesterol levels of rats fed the control, BD and glycerol diets. However, the liver lipids of the cold exposed BD fed rats, as well as the PG fed rats, were significantly ($P < 0.05$) increased as compared to the controls in the same environment.

When the rats were fed the 4 diets for 5 weeks and placed in the intense cold of -20°C, the number of hours 50% of each group survived is illustrated by the negative regression lines in Fig. 2. Rats consuming the glycols, (BD or PG) withstood the cold only about one-half as long as rats fed the 30% fat control or the glycerol diet. An analysis of variance of these data with a comparison of slopes (b values) of each line with the control group showed that the survival rate was significantly ($P < 0.05$) decreased when rats were fed the BD or PG diet. Feeding glycerol produced a survival rate similar to that of the controls. These findings suggest that further studies along this line may yield information applicable to the design of rations for use under low-temperature conditions.

The amount of epididymal adipose tissue of rats at either 25°C or 5°C (Table 5) appears to be correlated with the resistance of the animals to extreme cold. It is postulated from this experiment that the quantity of adipose tissue is a good indication of the animals' resistance to intense cold.

Skin resistance and electromyogram measurements were taken in rats fed the control 30% fat diet and BD at 25°C and 5°C. Normal increased skin resistance and shivering occurred in both groups of rats placed in the cold, indicating that rats consuming BD can initially respond to a lowered temperature.

From these studies, it is apparent that feeding relatively large amounts of specific non-toxic glycols as a source of calories, although they can be used for growth, decreases the quantity of adipose tissue lipids; this could be a causative factor in decreasing the resistance of the rat to intense cold. The mechanism whereby propylene glycol produces elevated liver lipids and liver cholesterol is unknown.

TABLE 5

Epididymal Adipose Tissue Weight, Liver Lipids, and Liver Cholesterol of Rats Fed Different Polyols for 4 Weeks at 2 Environmental Temperatures

	30% Fat		1,3-Butanediol		Propylene Glycol		Glycerol	
	25°C	5°C	25°C	5°C	25°C	5°C	25°C	5°C
Epid. Adipose Tissue[1] (g/100 g body wt)	1.127±0.11^{a}[2]	0.71±0.06^{b}	0.84±0.02^{b}	0.41±0.04^{c}	0.89±0.05^{b}	0.49±0.04^{c}	1.38±0.12^{a}	0.78±0.05^{b}
Liver Lipids (mg/g liver)	68.19±6.20^{bc}	52.01±2.33^{d}	76.01±5.21^{b}	68.43±2.82^{bc}	99.50±3.45^{a}	73.50±3.41^{bc}	60.19±5.36^{cd}	62.79±2.00^{cd}
Liver Cholesterol (mg/100 g Liver)	2.38±0.20^{cd}	2.28±0.07^{cd}	2.84±0.26^{c}	2.88±0.08^{c}	6.63±0.41^{a}	3.52±0.20^{b}	2.42±0.09^{cd}	2.03±0.13^{d}

[1] Dry weight.

[2] Mean ± SE. Means having a common letter in superscript are not significantly different ($P > 0.05$).

Lipid Distribution in Rats Fed 1,3-Butanediol. Previous investigations suggested that feeding BD and PG to rats as a carbohydrate replacement influences metabolism of lipids. Whether the BD effects on lipid metabolism is general, affecting all classes of tissue lipids, or whether it interferes with a particular lipid class is not known. In this section, the effects of prolonged feeding of BD as a replacement of "natural" carbohydrate on the individual lipid components of plasma of laboratory rats are reported.

As shown in Table 6, both increase in dietary fat and the presence of BD resulted in increased plasma FFA, triglycerides and cholesterol ester. However, the free cholesterol content of plasma did not respond to changes in dietary fat levels or the addition of BD.

TABLE 6
Distribution of Plasma Lipids in Rats Fed 1,3-Butanediol[1]

Diet	Tri-glycerides	Free Fatty Acids (FFA)	Cholesterol	
			Free	Ester
	mg%	mg%	mg%	mg%
10% Fat	12	30	27	72
30% Fat	32	58	22	76
30% Fat + 20% BD	46	68	22	108

[1] 5-week feeding.

Plasma FFA represents the form in which fatty acids are mobilized from the fat depots and transported to other tissues. In the fasted state, fatty acid metabolism is geared to provide substrate for oxidation by the tissues and there is a large net flux of FFA from adipose tissue to other tissues. In the results reported here, the elevated plasma FFA level in both groups receiving BD indicates that a greater mobilization of lipid from adipose tissue occurred in these animals. This was further evident when one observed the smaller fat pads and, consequently, lower lipid levels in these animals.

Liver is the site of synthesis of plasma low-density lipoprotein and in the post-absorptive state, it constitutes the major source of plasma triglycerides. Any impairment in the ability of liver to transport lipoproteins into the blood would cause a decrease in plasma lipids and a concomitant increase in the lipid content of liver. The higher plasma triglyceride levels in BD-fed rats indicate that the ability to transport low density lipoprotein from the liver to plasma is not impaired.

Influence of Feeding 1,3-Butanediol in the Dog. The endurance capacity of the dogs, as indicated by treadmill running to exhaustion, is presented in Fig. 3. At the end of 5 weeks, two dogs fed the BD diet (Dogs number 1 and 5), as well as the control fed dogs, increased their 5-week endurance capacity over that of their initial performance. Thus, both the 20% BD diet and the 30% fat control diets supported a similar level of sustained physical exercise in dogs.

As shown in Fig. 4, plasma free fatty acids increased in the dogs after consuming the BD diet for one week and remained at a 2-fold elevated level for the 5 week experimental period. After exhaustive exercise, the circulating free fatty acid increased about 6-fold in all dogs (Fig. 5). However, dogs fed the BD diet still had consistently higher levels of free fatty acids compared to dogs fed the control diet. Thus, in both the rat and the dog, certain lipids are increased in the plasma when BD is fed.

The results of a timed serial blood glucose study of dogs fed 30% BD and conducted during treadmill running is presented in Table 7. Plasma glucose increased in all dogs after exercise began. The plasma glucose of the BD fed dogs was initially higher than the controls, but both groups increased to the same magnitude at 80 minutes of exercise. However, at exhaustion the average plasma glucose of BD fed dogs was further increased, but that of the controls dropped.

TABLE 7

Plasma Glucose of Exercised Dogs Fed 1,3-Butanediol

Time of Exercise (min)	Dietary Treatment	
	30% BD + 30% Fat (mg/100 ml)	30% Fat Controls
0	115±2[1]	102±8
5	129±8	115±4
10	132±8	118±3
20	134±7	117±9
40	139±11	139±15
80	154±12	144[2]
Exhaustion	172±12	112[2]

[1] Std. Error of Mean
[2] 2 Dogs

PROJECTED APPLICATIONS

Energy-dense compounds can be recommended as a new approach to achieving nutritionally and logistically efficient diets. Actual savings in weight and volume will depend on the caloric value of the compound and the level incorporated in the ration. For example, the ultimate would be development of compounds with 9 kcal/gm or more, and their use to replace all of the approximately 1350 kcal now

supplied by carbohydrates. Such diets containing about 85% of their caloric content in the form of fat and high-energy compounds could be expected to provide daily caloric needs in a food packet weighing less than one pound in a volume of less than 400 cm^3. This is, of course, a desired goal and not within current capability.

To obtain almost complete nutritional utilization, the synthetic food compounds should be used in diets containing no fiber and other materials which are poorly digested or absorbed. In addition, the diet should be designed to meet the specific metabolic needs of man without supplying unnecessary or undesirable exesses. Diet design should be based on carefully controlled metabolic studies conducted under specific environmental and stressful conditions.

The synthetic compounds can also be considered for use as functional supplements in conventional foods or as major caloric components of "tailor made" or formula type diets. By application of creative food technology, a number of acceptable food items can be developed. Palatability may present some problems and require skillful blending of flavors and other components. In addition, modern encapsulation techniques may be useful in allowing incorporation of liquid compounds into solid forms of food. Liquid food compounds could also be encapsulated into the core of bite-size food items. All food compounds used must, of course, be of food grade purity and be approved for food use by the Food and Drug Administration.

SUMMARY

Data have been presented to show that synthetically produced 1,3-butanediol, propylene glycol and glycerol, which are not normal food sources, can be used to supply dietary calories. All 3 compounds were utilized by animals under a variety of experimental conditions. The results obtained indicate that many problems remain, but that these compounds can serve as models. Nevertheless, the data support the concept that other more potentially useful food compounds can be found, designed, or synthesized. Such compounds, therefore, offer a new approach in the development of nutritionally and logistically ultra-efficient, "tailor designed", combat rations of the future. At the same time, development of a means of producing food completely independent of land cultivation may serve to promote international stability and peace by counteracting hunger among the world's rapidly multiplying peoples.

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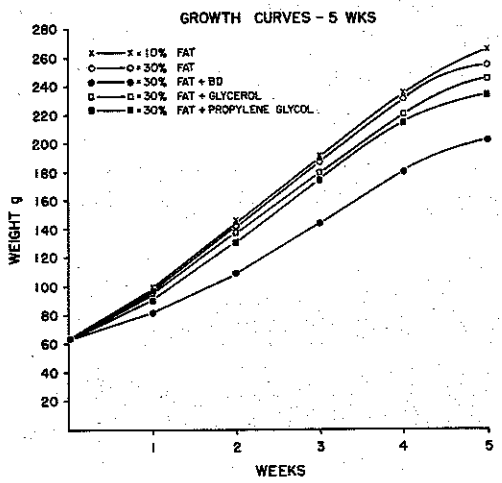

Fig. 1. Growth of rats fed various polyhydric alcohols.

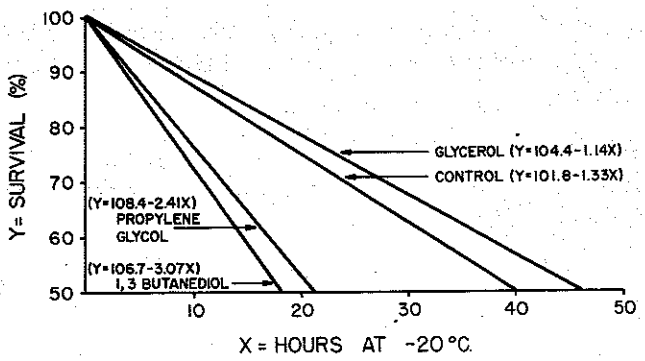

Fig. 2. Regression lines showing percent survival (Y) of rats fed polyhydric alcohols at various hours (X) of exposure to -20°C cold. Control fed 30% Fat; all diets fed 5 weeks prior to cold exposure.

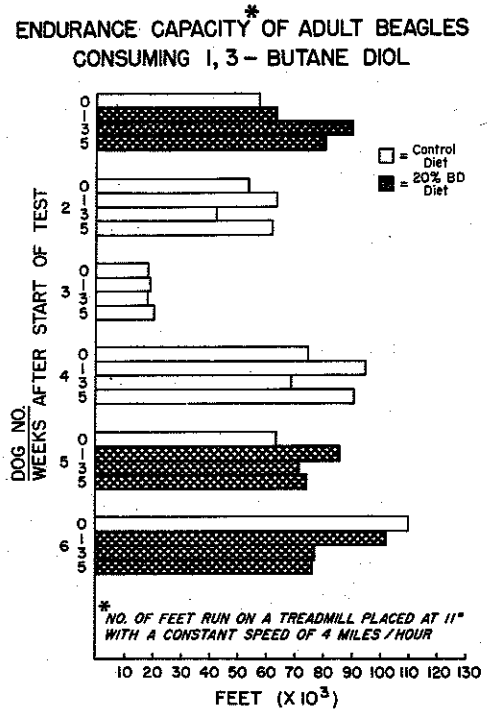

Fig. 3. Endurance capacity of dogs fed 1,3-butanediol.

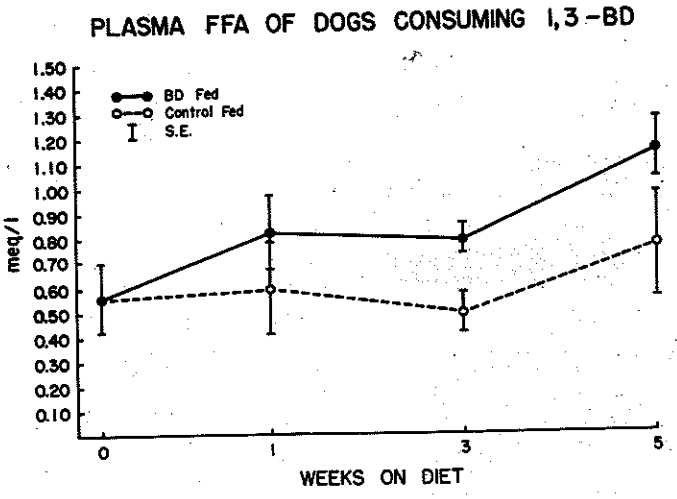

Fig. 4. Before exercise plasma free fatty acids of dogs fed 1,3-butanediol.

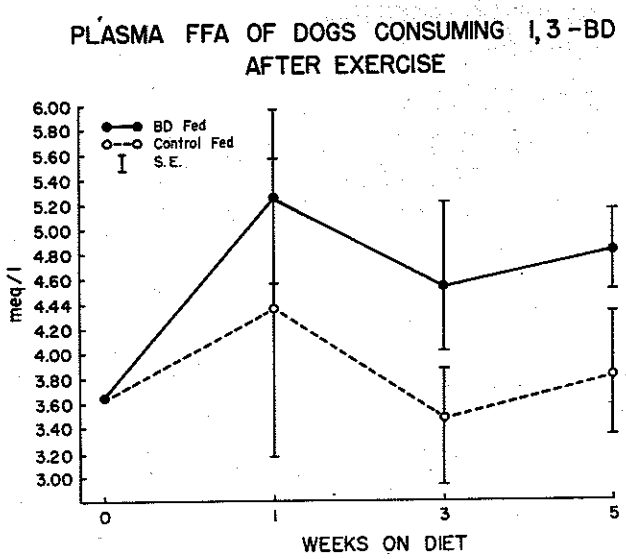

Fig. 5. Plasma free fatty acids of dogs fed 1,3-butanediol after exercise to exhaustion.